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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,131	09/30/2003	Robert F. Balint	021167-001100US	3895

20350 7590 02/23/2006

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/677,131	BALINT ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-32,38,40-47,53 and 55-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37,39,48-52 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group III (claims 33-62) in the reply filed on 11/7/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' election of the following species: A). Fab fragment for a candidate binding molecule, B). scFv for a competitor is also noted. Applicants state that claims 33-37,39, 43-52, 54 and 58-62 reads on claim A species while claims 33-35, 37-45, 48-50 and 52-60 reads on the B species. However, the claims that read on the elected species are listed below under the status of the claims.

Status of Claims

Claims 1-62 are pending

Claims 1-32, 38, 40-47, 53 and 55-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 33-37, 39, 48-52 and 54 are under examination.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors

(typographical, grammatical and idiomatic). Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-37, 39, 48-52 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicants have invented species sufficient to constitute the gen[us]. Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004).

The specification does not provide adequate written description for the claimed method comprising the broad steps using broad components. The description in the specification relates to a single species for each of the broad components. For example, a b-lactamase as the responder molecule and antibodies (Fab or scFv) for target and candidate binding molecules. There is no correlation of these species to the huge scope of the claimed components of the method. It does not describe a library of genes comprising the responder complex, the target binding ensemble linked to a reactivator complex and other undefined structures of the other components. For example, it does not describe the kind, length or

size or other qualifying features of the library of genes. The specification provides only definitions for each of these components of the method. The detailed description of the invention relates to a method using specific, defined components of the huge claimed components. There is no indication in the specification as to the applicability of the single embodiment to the different components of unspecified feature, as claimed. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993. See also, See University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-37, 39, 48-52 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is indefinite for missing an essential step. Step(a) uses a competitor, the last step (c) does not recite for any competitor. Also, it is confusing as to the attachment of the responder inhibitor. Cf. with Fig.1 and Fig. 3. The target contains the inhibitor responder instead of the library expressing genes. The use of terminologies e.g., "reactivator complex" and "auto-inhibited responder" are not consistent with those art. Also, the used of inconsistent terminologies provide for confusion and ambiguity. For example, "competitor" and "reference." It is suggested that applicants utilize terminologies consistent with the art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting

rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-37, 39, 48-52 and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/208,730 ('730 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed method is encompassed by the broad claimed method of the '730 application. The instant claimed method which recites a recombinant method would be included in the broad method of the '730 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-37, 39, 48-52 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Dove et al (USP 5,925,523).

Dove discloses at col. 4, lines 1-24 a method for detecting interaction between a first test polypeptide (library of gene expressing proteins, as claimed) and a second test polypeptide (target). The method comprises a step of providing an interaction trap system including a prokaryotic host cell, which contains a reporter gene operably linked to a transcriptional regulatory sequence, which includes a binding site ("DBD recognition element") for a DNA-binding domain. The cell is engineered to include a first chimeric gene which encodes a first fusion protein, the first fusion protein including a DNA-

binding domain and first test polypeptide. The cell also includes a second chimeric gene which encodes a second fusion protein including an activation tag (such as a polymerase interaction domain [PID]) and a second test polypeptide. Interaction of the first fusion protein and second fusion protein in the host cell activates transcription of the reporter gene, e.g., results in measurably greater expression of the reporter gene. See also, col. 16, lines 30-50, which describes the variegated library of nucleic acids. Dove at col. 19, lines 45-60 discloses the antibody e.g., sc antibodies. The markers are discloses at col. 22, lines 26-36. The method also includes the steps of measuring expression of the reporter gene, and, generally, comparing the level of expression of the reporter gene to a level of expression in a control interaction trap system. A statistically significant increase in the level of expression is indicative of an interaction between the first and second test polypeptide portions of the fusion proteins. Dove at col. 23, lines 12-63 an auto-inhibited responder complex as claimed. It discloses a bait and prey proteins positively regulate expression of the first reporter gene. Accordingly, where the first reporter gene is a repressor of expression of the second reporter gene, relieving expression of the first reporter gene by inhibiting the formation of complexes between

the bait and prey proteins concomitantly relieves inhibition of the second reporter gene. For example, the first reporter gene can include the coding sequences for lambda.cI. The second reporter gene can accordingly be a positive signal, such as providing for growth (e.g., drug selection or auxotrophic relief), and is under the control of a promoter which is constitutively active, but can be repressed by lambda.cI. In the absence of an agent which inhibits the interaction of the bait and prey protein, the lambda.cI protein is expressed. In turn, that protein represses expression of the second reporter gene. However, an agent which disrupts binding of the bait and prey proteins results in a decrease in lambda.cI expression, and consequently an increase in expression of the second reporter gene as lambda.cI repression is relieved. Hence, the signal is inverted. The method also discloses detecting agents which disrupt the bait-prey interaction, it is envisioned that under certain conditions the interaction between bait and prey fusion proteins might result in transcription repression rather than activation. For example, it is speculated that sufficiently strong binding between a bait fusion protein and a prey fusion protein may impede the escape of the polymerase from the promoter, which escape is required for elongation of a transcript, thus repressing transcription. In particular, a

strong interaction between the bait and prey proteins, combined with a strong promoter (e.g., one which is efficient at binding the polymerase complex even in the absence of transcription factors) may result in repression of reporter gene expression. Under these conditions an inhibitor of bait-prey complex formation will, over a certain concentration range, cause the effective association constant of the complex to be reduced sufficiently to result in relief of the repression and concomitant transcription of the reporter gene. At higher concentrations, inhibitors of the bait-prey complex may result in inhibition (or return to basal levels) of transcription by the loss of bait-prey complexes. Thus, in one embodiment, the candidate agent can be spotted on a lawn of reagent cells plated on a solid media. The diffusion of the candidate agent through the solid medium surrounding the site at which it was spotted will create a diffusional effect. For agents which inhibit the formation of bait-prey complexes, a halo of reporter gene expression would be expected in an area which corresponds to concentrations of the agent which offset the effect of the repression due to strong association between the two hybrid proteins, but which are not so great as to substantially inhibit the formation of bait-prey complexes. See specifically the Examples at col. 29, line 35 up to col. 32, line 9 that

describes in detail the method. Accordingly, the specific method steps of Dove employing specific components fully meet the broad claimed invention.

Claim Rejections - 35 USC § 103

Claims 33-37, 39, 48-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balint (WO 00/71702) in view in view of Strynadka et al (Nature) or Yanagawa et al (2005/0142623).

Balint et al teaches a method of detecting protein interactions or inhibitors of these interactions using a fragment complementation system which is characterized by using reporter fragment pairs fused to a first and a second member, wherein binding of the first polypeptide to the second polypeptide results in the functional reconstitution of the fragment pair into a marker protein, and the interaction of the two polypeptides can be detected. Thus, folding of the responder enzyme from its fragments is catalyzed by the binding of the test proteins to each other, and is detected as reconstitution of enzyme activity. Balint et al also teaches appropriate host cells for the application of the subject inventions, which include the bacterial cell population such as Escherichia Coli (a gram negative bacteria). Balint et al also

teaches examples wherein the polypeptide interactor domains can be selected from (i) single-chain antibody Fv fragments (scFv) (see example 1 in particular), wherein scFv is comprised of antibody heavy chain and light chain variable regions (VH and VL) tethered into a continuous polypeptide by a inker or (ii) an antibody light chain V-regions (VL) (see example 2 in particular and (iii) the reporter fragment molecules to be the b-lactamase G197 and 0198 fragments (interaction-dependent YEM-I b-lactamase fragments). When the two vectors (fusion proteins), as mentioned above, are expressed in a bacterial cell the two p-lactamase fragments cooperatively produce selectable activity in a manner that is strictly dependent on the specific interaction between the two polypeptides domains. Thus, if a fragment pair library of a non-phenotypic protein is expressed as fusions to the interaction-dependent TEM-I (b-lactamase fragments), it is expected that only those fragment pairs (the polypeptide domains) which associate and fold into the native conformation will provide sufficient docking function to facilitate selectable p-lactamase activation. Balint et al further teaches that such target interactions identified using interaction-dependent lactamases could be used to screen for inhibitors of the interaction of the two polypeptide interactor domains (see page 20, lines 9-1 1 in particular). Thus Balint et al teaches a

system in which a target molecule is identified in a bacterial cell population, wherein the target molecule may inhibit the interaction between two polypeptide interactor domains and the inhibition of interaction is indicated by the absence of the b-lactamase activation. Balint et al does not specifically teach the method wherein the polypeptide domains are linked to a reporter and an inhibitor of the reporter molecule, wherein the activation of the reporter molecule indicates the inhibition of the interaction of polypeptide domains and vice versa. However, Strynadka et al teaches a TEM-I lactamase inhibitor protein (BLIP). The ability of BLIP to adapt to a variety of b-lactamases is most likely due to an observed flexibility between two domains of the inhibitor and to an extensive layer of water molecules entrapped between the enzyme and inhibitor (see abstract, in particular). Strynadka et al teach the inhibition of b-lactamases by BLIP using crystallographic studies including that the kinetic analyses of BLIP with a wide spectrum of p-lactamases characterize it as the most potent inhibitor of the enzyme. Yanagawa et al discloses at page 7, Example 1 a b-lactamase and complex of b-lactamase and b-lactamase inhibitory protein(BLIP) (referring to Strynadka). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use BLIP in the method of

Balint as taught by Strynadka or Dove for the advantage in the use of a complex b-lactamase and BLIP. This advantage would provide the motivation to one having ordinary skill in the art at the time the invention was made to make said modification.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0812. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw

February 17, 2006